REMARKS

Applicants submit this Reply in response to the Final Office Action dated December 31, 2002. Claims 19-29 are pending and under consideration. Favorable reconsideration of the subject application is respectfully requested in view of the remarks provided herein.

Rejection under 35 U.S.C. § 103(a)

Claims 19-29 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Van Eldik *et al.*, Okada *et al.*, and Shibue *et al.* More specifically, the Action alleges that Van Eldik *et al.* teaches two different monoclonal antibodies specific for S100β, Okada *et al.* teaches dual antibody ELISAs wherein the antibodies are bound to a magnetic particle carrier, and Shibue *et al.* teaches dual antibody ELISAs wherein the immunoreactant measurement is performed via electrochemiluminescence using luminol. The Action concludes that it would, therefore, have been obvious to the skilled artisan to use the monoclonal antibodies of Van Eldik *et al.* in the dual antibody ELISA assays of Okada *et al.* and Shibue *et al.* using magnetic carrier immobilization and detection via chemiluminescence. The Action further asserts that the skilled artisan would have been motivated to perform such a dual antibody ELISA assay based upon the advantages taught by Okada *et al.* and Shibue *et al.* and would have expected positive results based upon the success achieved in the cited references and the high degree of skill in the relevant art.

Applicants respectfully traverse this basis of rejection and submit that the cited references, alone or in combination, fail to teach each element of the claimed invention. Furthermore, Applicants submit that the cited references would not motivate the skilled artisan to achieve the claimed invention. Accordingly, Applicants submit that the cited references do not anticipate claims 19-29.

As an initial matter, Applicants note that the claimed invention is directed to methods and kits comprising two distinct monoclonal antibodies, each specific for different

regions of S100β. Applicants respectfully submit that careful examination of Van Eldik *et al.* reveals that this reference fails to teach two distinct monoclonal antibodies specific for S100β. Instead, the overwhelming evidence demonstrates that the two monoclonal antibodies produced by Van Eldik *et al.* are identical. As described in Van Eldik *et al.*, two antibody-producing hybridomas were identified that secreted monoclonal antibodies that appeared to be specific for S100β. However, further analysis of these hybridomas revealed that they produce the same antibody. As stated on page 6035, column 2, paragraph 5, "[b]oth monoclonal antibodies are of the IgG1k isotype. In all characterizations done to date, the two monoclonal antibodies are indistinguishable in their reactivities." The fact that the authors believed that the two hybridomas produced the same antibody is further evidenced by the fact that all of the experiments described in Van Eldik *et al.* were performed using a single antibody. Accordingly, Van Eldik *et al.* fails to teach two distinct monoclonal antibodies that bind different regions of S100β, as currently claimed. Okada *et al.* and Shibue *et al.* clearly fail to remedy this deficiency, as they provide no description of monoclonal antibodies to S100β.

Applicants further submit that the ability of Van Eldik *et al.* to produce a single monoclonal antibody specific for S100β would not motivate the skilled artisan to attempt to develop a dual antibody ELISA assay for S100β. Indeed, the fact that Van Eldik *et al.* were unable to produce more than one antibody specific for S100β from 10^8 spleen cells isolated from immunized mice would discourage the skilled artisan from attempting to develop any assay requiring two distinct antibodies specific for S100β. Furthermore, the skilled artisan would recognize that, given the small size of the S100β polypeptide and its substantial homology to other S100 polypeptides, the number of S100β specific epitopes present in the S100β polypeptide is probably very small. Indeed, the teachings of Van Eldik *et al.* strongly suggest that only a single S100β specific epitope is present in the entire polypeptide. Thus, the skilled artisan, based upon the teachings of Van Eldik *et al.*, would have no reasonable expectation of being able to successfully produce two distinct monoclonal antibodies against S100β, as required to perform the claimed method or produce the claimed kit. Therefore, Van Eldik *et al.* actually teaches away from the claimed invention.

Applicants respectfully submit that the combined disclosure of Van Eldik *et al.*, Okada *et al.*, and Shibue *et al.*, cannot reasonably render obvious to the skilled artisan the currently claimed invention, since the combined disclosure of these references fails to teach, suggest, or otherwise motivate a skilled artisan to arrive at Applicants' methods employing two distinct S100β antibodies that are specific for two distinct epitopes of the S100β protein. As additional support for this conclusion, the accompanying Declaration of Anne-Charlotte Aronsson is provided. Reconsideration and withdrawal of this rejection is thus respectfully requested.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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WTC:jto

Enclosure:
Postcard
Notice of Appeal (+ copy)
Declaration of Anne-Charlotte Aronsson

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